

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/IB2004/003897

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C12N9/64 C07K14/47

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, Sequence Search, SCISEARCH, CHEM ABS Data, LIFESCIENCES, WPI Data, PAJ, MEDLINE, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>SALANOUNAT M ET AL: "Genome sequence of the plant pathogen <i>Ralstonia solanacearum</i>"  <i>NATURE (LONDON)</i>,  vol. 415, no. 6871,  31 January 2002 (2002-01-31), pages  497-502, XP002317761  ISSN: 0028-0836  the whole document</p> <p>-----</p> <p>DATABASE EMBL  10 September 2001 (2001-09-10), "Human  aspartyl protease ASP-2"  XP002317765  retrieved from EBI  Database accession no. AAE04797  abstract; figure 1</p>	3, 4
X		1, 2, 4, 6, 8, 10-15, 23

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

16 February 2005

Date of mailing of the international search report

09/03/2005

Name and mailing address of the ISA  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	& WO 01/46398 A (INCYTE GENOMICS, INC; KASER, MATTHEW, R; COCKS, BENJAMIN, G; LORING, J) 28 June 2001 (2001-06-28) figure 1 examples 1,7,12 ----- FUJIWARA HIROSHI ET AL: "Neutrophil Elastase: A Candidate Antigen for Adoptive T Cell Therapy for Myeloid Leukemia?" BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 2666, XP009044091 & 44TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HEMATOLOGY; PHILADELPHIA, PA, USA; DECEMBER 06-10, 2002 ISSN: 0006-4971 abstract ----- ZOHAR OFER ET AL: "Quantification and distribution of beta-secretase alternative splice variants in the rat and human brain." MOLECULAR BRAIN RESEARCH, vol. 115, no. 1, 4 July 2003 (2003-07-04), pages 63-68, XP002317763 ISSN: 0169-328X the whole document ----- TANAHASHI HIROSHI ET AL: "Three novel alternatively spliced isoforms of the human beta-site amyloid precursor protein cleaving enzyme (BACE) and their effect on amyloid beta-peptide production" NEUROSCIENCE LETTERS, vol. 307, no. 1, 6 July 2001 (2001-07-06), pages 9-12, XP002317764 ISSN: 0304-3940 cited in the application the whole document ----- EHEHALT ROBERT ET AL: "Splice variants of the beta-site APP-cleaving enzyme BACE1 in human brain and pancreas" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 293, no. 1, 26 April 2002 (2002-04-26), pages 30-37, XP002317938 ISSN: 0006-291X page 30, column 2, paragraph 2 - page 31, column 1, paragraph 1 -----	15-18, 24  1-14, 19-23  1-14, 19-23  1-14, 19-23
		-/-

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>TURNER R T ET AL: "SUBSITE SPECIFICITY OF MEMAPSIN 2 (BETA-SECRETASE): IMPLICATIONS FOR INHIBITOR DESIGN"            BIOCHEMISTRY, AMERICAN CHEMICAL SOCIETY.            EASTON, PA, US,            vol. 40, no. 34,            28 August 2001 (2001-08-28), pages            10001-10006, XP001095820            ISSN: 0006-2960            the whole document</p> <p>-----</p>	15-18,24
A	<p>HOM R K ET AL: "Design and synthesis of statine-based cell-permeable peptidomimetic inhibitors of human beta-secretase"            JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US,            vol. 46, no. 10, 8 May 2003 (2003-05-08),            pages 1799-1802, XP002262787            ISSN: 0022-2623            the whole document</p> <p>-----</p>	15-18,24

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claim 19 is directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 17 and 18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: 12,15,16,24

Present claims 16 and 24 relate to a product/compound defined by reference to a desirable characteristic or property, namely to bind or to inhibit BACE455.

The claims cover all products/compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products/compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims 12, 15, 16 and 24 which appear to be clear, supported and disclosed, namely those parts relating to antibodies directed against BACE455 as well as the inhibitors Brefeldin A and Gleevec.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2.  Claims Nos.: 12, 15, 16, 24  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

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Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 0146398	A	28-06-2001	US 2002169304 A1	14-11-2002
			AU 2093301 A	03-07-2001
			CA 2395286 A1	28-06-2001
			EP 1252299 A2	30-10-2002
			JP 2004500811 T	15-01-2004
			WO 0146398 A2	28-06-2001

**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/IB2004/003897**Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - a sequence listing
    - table(s) related to the sequence listing
  - b. format of material
    - in written format
    - in computer readable form
  - c. time of filing/furnishing
    - contained in the international application as filed
    - filed together with the international application in computer readable form
    - furnished subsequently to this Authority for the purpose of search
2.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments: